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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,833	09/19/2003	Andrew H. Segal	85849DIV4(308597)	6845

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EXAMINER	
BLUMEL, BENJAMIN P	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,833	SEGAL ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/13/2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-14* is/are pending in the application.

5a) Of the above claim(s) *4* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-3 and 5-14* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3 and 5-14 are examined on the merits. Claim 4 remains withdrawn as it is drawn to a non-elected species.

Response to Arguments

Applicant's arguments filed 6/13/2011 have been fully considered but they are not persuasive. See responses below.

Double Patenting

In response to the double patenting rejections set forth in the previous office action, and restated below, Applicant submits that upon notification of otherwise allowable subject matter in the instant case, Applicants will address the double patenting rejections.

Applicant's intention is noted. However, until the rejections are properly addressed, with the submission of a terminal disclaimer, all double patenting rejections are maintained for the reason(s) set forth in the record.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed.

Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(Prior Rejection Maintained) Claims 1-3 and 5-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5-12 of copending Application No. 10/666,886. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and the invention of the co-pending application are drawn to variations of a composition which contains an antigen bearing target, such as a mammalian cell and a fusion polypeptide that contains either an amino acid sequence that binds to a carbohydrate or a sequence that comprises a cell-surface binding moiety fused to a ligand for a GM-CSF receptor on the surface of a leukocyte. As a result, the claimed invention of '886 renders the instant invention obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(Prior Rejection Maintained) Claims 1-3 and 5-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-14 of U.S. Patent No. 7,629,440 (US Patent Application 10/224,661). Although the conflicting claims are not identical, they are not patentably distinct from each other because while the patented invention is drawn to a fusion polypeptide with a first amino acid sequence containing an influenza virus Hemagglutinin protein (a protein that binds to a sialic acid on the surface of a cell) and a second amino acid sequence of a GM-CSF molecule that can bind to its receptor, the disclosure of '440 also teaches a method of using a composition containing such a fusion protein linked to an antigen bearing target, such as a mammalian cell that cannot divide, more specifically a leukocyte or antigen presenting cell in a composition. This same composition can also contain the fusion protein not linked to the antigen bearing target. (See Columns 9 and 10). This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims.

Therefore, since the patented invention and the teachings of its disclosure produce the claimed composition, the instant invention is obvious to one of ordinary skill in the art.

Response to arguments:

Applicants state that upon notification of otherwise allowable subject matter in the instant case, they will address the double patenting rejections.

Claim Rejections - 35 USC § 112

(New Rejection Necessitated by Amendments) Claims 8 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites, "...said cell divides at a rate that is less than about 50% of the rate of division of corresponding cells which are not treated to prevent division." Therefore, the examiner is interpreting claim 8 to actually state that the cells employed in the composition have been treated to prevent division. Based on this interpretation, it is unclear how a cell that has been treated to prevent division can still divide as implied by the claim [i.e., "...cell divides at a rate that is less than about 50%..."]. Claim 14 also recites similar limitations as in claim 8 and therefor is also indefinite.

Claim Rejections - 35 USC § 102

(New Rejection) Claims 1-3, 5-7 and 9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoo (US Pat. 5,891,432) as evidenced by Varki (PNAS, 1994).

The claims are directed to a composition comprising a mammalian cell (antigen bearing target), and a fusion polypeptide comprising i) a first amino acid sequence that can bind a carbohydrate and ii) a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte. The composition also includes the cell and the

fusion polypeptide being bound via a carbohydrate on said cell and a polypeptide not bound to the cell. Claim 2, which depends on claim 1, limits the second amino acid sequence to a ligand for a cytokine receptor, which is limited to GM-CSF by claim 3. Claim 5, which depends on claim 1, requires the cell to be a mammalian cell. Claim 6, which depends on claim 5, requires the cell to be a pathogenic cell. Claim 7, which depends on claim 5, requires the cell to be an attenuated cell. Claim 9, which depends on claim 1, requires the leukocyte to be an antigen presenting cell, which is specified as a professional antigen presenting cell by claim 10 and dendritic cell by claim 11. In addition, the first amino acid sequence can bind to a sialic acid on a glycoprotein or it can comprise a carbohydrate-binding domain of a naturally occurring lectin (claims 12 and 13).

The Prior Art

Hoo teaches a composition comprising a cell (antigen bearing target) and a fusion polypeptide containing a membrane attachment domain and cytokine which is a ligand for a cytokine receptor. Hoo also teaches that the composition can contain the fusion protein attached to the cell and a soluble secondary immunomodulatory molecule, such as a cytokine (i.e., protein) in a membrane bound form or in a soluble form (see column 18, lines 33-62). The antigen bearing target that Hoo teaches includes a virus, a bacterial cell, fungal cell, a cell of a parasite, a mammalian cell, pathogenic and attenuated antigens, and a cell that is substantially unable to divide. [Lines 35-45, column 10, and columns 9-18, in particular.]

The first amino acid sequence in the fusion polypeptide of Hoo comprises the sequence to a membrane attachment domain, a cell-surface binding moiety, such as a

domain that spans the width of a cell membrane or any part thereof that would attach the fusion protein to the cell surface. Specific examples of the membrane attachment domains are: CD molecules; a phosphatidylinositol-glycan anchor that binds to the CT domain of a cell membrane protein; and selectins [See columns 7-8]. Based on the teachings of Varki (PNAS, 1994), selectins are naturally occurring lectins which bind to sialylated glycoproteins [see page 7390 of Varki]. The second amino acid sequence in the fusion polypeptide of Hoo comprises the sequence of a ligand for a cell surface polypeptide of a leukocyte. Specifically, the ligand for a cell surface polypeptide of a leukocyte is a ligand for a cytokine receptor. In particular, the ligand for a cytokine receptor that Hoo et al. teaches is GM-CSF [Example I, column 22, in particular.] The ligand for a cell surface polypeptide used by Hoo is a ligand for a cell surface polypeptide of a leukocyte, wherein the leukocyte is dendritic cells, which is a professional antigen presenting cell [Columns 1-2, in particular.]

Therefore, since Hoo teaches the generation of fusion proteins which comprise membrane attachment domains (such as selectins) or parts thereof and ligands for leukocyte cell surface polypeptides (such as GM-CSF) and the immobilization of the fusion protein on the surface of cells in the formulation of a cellular vaccine composition, Hoo anticipates the instant invention.

Response to arguments:

Applicant presents the following arguments in traversal of the rejection:

As stated by the Examiner in the previous Office action, Hoo fails to teach or suggest that a fusion protein is bound to a carbohydrate of a cell via the first amino acid

sequence of the fusion protein. In addition, Hoo fails to teach that the fusion protein is both bound and unbound to the cell as part of the same composition.

It is also argued that applicants have discovered that compositions comprising bound and free fusion polypeptide, when bound fusion polypeptide is bound to a carbohydrate on a cell via a cell-binding moiety are effective at modulating an immune response. Applicants further point to Examples 18 and 19 which present murine *in vivo* administration methods of GM-CSF-HA1 fusions proteins which are attached to melanoma cells and in unattached form reduce metastatic tumor numbers and/or increase the number of tumor free mice. Therefore, applicants are the first to appreciate the dual administration of bound and unbound fusion protein was effective in vaccinating mice against tumor development.

Rebuttal:

In response, since Hoo teaches that selectins (naturally occurring lectins that bind to sialylated glycoproteins) or portions thereof can be used in fusion proteins in conjunction with cytokines, such as GM-CSF, and that cells can be formulated with these fusion proteins immobilized, Hoo anticipates the instant invention. Furthermore, Hoo et al. teach the administration of cells with immobilized GM-CSF and that they do not teach washing these cells prior to administration. Therefore, unbound GM-CSF was also present in the composition that is to be administered to the host.

With regard to applicants findings of better results when both bound and unbound fusion protein was administered to mice in treating tumors, since Hoo teaches that such a composition can be generated and that washing of this composition is not necessary prior

to administration, both bound and unbound fusion proteins would be administered to the target host. Furthermore, the instant invention is presently drawn to a composition of bound and unbound fusion proteins that is suitable for administration to a subject. Therefore, is applicant is attempting to present unexpected results, the specific products employed by applicants in achieving their results are presently not claimed. Therefore, these unexpected results are not commensurate in scope with the instant invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BENJAMIN P BLUMEL/
Primary Examiner, Art Unit 1648